

Christophe P.G. Gerald, et al.
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is considered timely filed under 37 C.F.R. §1.7. Accordingly, this Amendment is being timely filed.

Please amend the subject application as follows:

In the Claims:

Please cancel claims 178, ~~179~~ and ~~180~~ without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend claims 183-184 as follows:

--183. (Amended) A process for preparing a pharmaceutical composition which comprises determining whether a compound is a mammalian NPFF receptor agonist using the method of:

- C
- (a) contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor with the compound under conditions permitting the activation of the mammalian NPFF receptor, and detecting an increase in mammalian NPFF receptor activity, so as to thereby determine whether the compound is a mammalian NPFF receptor agonist;
 - (b) recovering the compound free of any mammalian NPFF receptor; and
 - (c) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.--

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--184. (Amended) A process for preparing a pharmaceutical composition which comprises determining whether a compound is a mammalian NPFF receptor antagonist using the method of:

- C1
- (a) contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor with the compound in the presence of a known mammalian NPFF receptor agonist, under conditions permitting the activation of the mammalian NPFF receptor, and detecting a decrease in mammalian NPFF receptor activity, so as to thereby determine whether the compound is a mammalian NPFF receptor agonist;
 - (b) recovering the compound free of any mammalian NPFF receptor; and
 - (c) admixing a pharmaceutically acceptable amount the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.--

Please add new claims 185-190 as follows:

--185. (New) A process for of preparing a pharmaceutical composition which comprises:

- C2
- (a) identifying a chemical compound which specifically binds to a mammalian NPFF receptor by a method which comprises contacting cells containing DNA encoding and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not

normally express the mammalian NPFF receptor, or a membrane preparation of such cells, with the chemical compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the mammalian NPFF receptor;

- (b) recovering the compound free of any mammalian NPFF receptor; and
- (c) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.


CN --186. (New) A process for preparing a pharmaceutical composition which comprises:

- (a) identifying a chemical compound which specifically binds to a mammalian NPFF receptor by a competitive binding method which comprises separately contacting cells containing DNA encoding and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, or a membrane preparation of such cells, with both the chemical compound and a second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the mammalian NPFF receptor, a decrease

in the binding of the chemical compound indicating that the chemical compound binds to the mammalian NPFF receptor;

- (b) recovering the compound free of any mammalian NPFF receptor; and
- (c) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

--187. (New) A process for preparing a pharmaceutical composition which comprises:

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- (a) identifying a compound that specifically binds to a mammalian NPFF receptor by a method which comprises contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, or a membrane preparation of such cells, with a compound known to bind specifically to the mammalian NPFF receptor;
 - (b) contacting the preparation of step (a) with a plurality of compounds not known to bind specifically to the mammalian NPFF receptor, under conditions permitting binding, and detecting specific binding of the compound known to bind to the mammalian NPFF receptor;
 - (c) determining whether the binding of the compound

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known to bind to the mammalian NPFF receptor is reduced in the presence of any compound within the plurality of compounds relative to the binding of the compound in the absence of the plurality of compounds; and if so


- (d) separately determining the binding to the mammalian NPFF receptor of compounds included in the plurality of compounds so as to thereby identify the compound which specifically binds;
- (e) recovering the compound free of any mammalian NPFF receptor; and
- (f) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

--188. (New) A process for preparing a pharmaceutical composition which comprises:

- (a) identifying a chemical compound which specifically binds to and activates a mammalian NPFF receptor by a method which comprises contacting cells producing a second messenger response and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with the chemical compound under conditions suitable for activation of the mammalian NPFF receptor, and measuring the second messenger

response in the presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound activates the mammalian NPFF receptor;

- (b) recovering the compound free of any mammalian NPFF receptor; and
- (c) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

 --189. (New) A process for preparing a pharmaceutical composition which comprises:

- (a) identifying a chemical compound which specifically binds to and inhibits activation of a mammalian NPFF receptor by a method which comprises separately contacting cells producing a second messenger response and expressing on their cell surface the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with both the chemical compound and a second chemical compound known to activate the NPFF receptor, and with only the second chemical compound, under conditions suitable for activation of the human NPFF receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of

both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the human NPFF receptor;

- (b) recovering the compound free of any mammalian NPFF receptor; and
- (c) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

--190. (New) A process for preparing a pharmaceutical composition which comprises:

- (a) identifying a compound that activates a mammalian NPFF receptor by a method which comprises contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with a plurality of compounds not known to activate the mammalian NPFF receptor;
- (b) determining whether the activity of the mammalian NPFF receptor is increased in the presence of such compounds; and if so
- (c) separately determining whether the activation of

the mammalian NPFF receptor is increased by each compound included in the plurality of compounds, so as to thereby identify the compound that activates the mammalian NPFF receptor;

- (d) recovering the compound free of any mammalian NPFF receptor; and
- (e) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

Ca-191. (New) A process for preparing a pharmaceutical composition which comprises

- (a) identifying a compound that inhibits the activation of a mammalian NPFF receptor by a method which comprises contacting cells transfected with and expressing DNA encoding the mammalian NPFF receptor, wherein such cells do not normally express the mammalian NPFF receptor, with a plurality of compounds in the presence of a known mammalian NPFF receptor agonist, under conditions permitting activation of the mammalian NPFF receptor;
- (b) determining whether the activation of the mammalian NPFF receptor is reduced in the presence of such plurality of compounds, relative to the activation of the mammalian NPFF receptor in the absence of

the plurality of compounds; and if so

(c) separately determining the inhibition of activation of the mammalian NPFF receptor for each compound included in the plurality of compounds is increased by each compound included in the plurality of compounds, so as to thereby identify the compound that inhibits the activation the mammalian NPFF receptor;

Cn (d) recovering the compound free of any mammalian NPFF receptor; and

(e) admixing a pharmaceutically acceptable amount of the compound with a pharmaceutically acceptable carrier, thereby preparing the pharmaceutical composition.

A marked-up version of the amendments showing the changes made is attached hereto as **Exhibit A**.